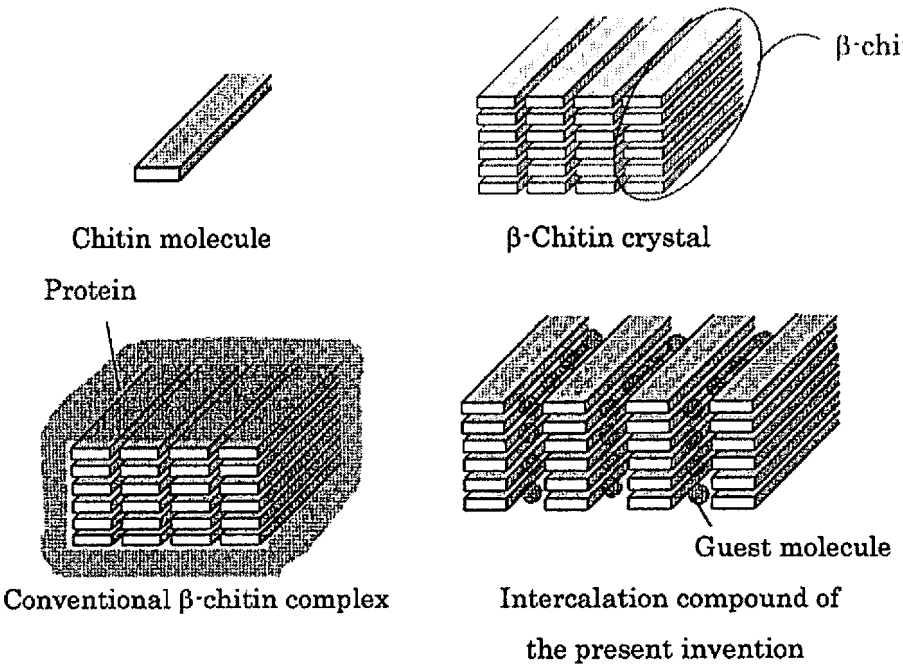
REMARKS

Claims 1-14 are pending in the application. Claims 8-14 have been withdrawn, and claims 1-7 are under consideration. Claims 1-7 are directed to a manufactured β-chitin complex comprising an intercalation compound formed by using as a host a β-chitin, and introducing a guest compound between the stacked sheets of chitin molecular chains forming the crystal lattice of the β-chitin. The only known naturally-occurring intercalation compound of β-chitin is an intercalation compound with water, i.e., a β-chitin hydrate. The Applicants have succeeded in manufacturing intercalation compounds of β-chitin with a guest compound as defined in independent claim 1, namely a guest compound "having a functional group that can form a hydrogen bond with a hydroxyl group and/or an amide group of the β-chitin and having a melting point of at least 60°C". The guest compound is a small polar molecule.

In the intercalation compound recited in the claims, the entire structure of the β-chitin crystal composed of chitin molecules is distorted as compared to the structure of a naturally occurring β-chitin crystal. The lattice spacing between the molecular sheets is increased by the interposition of the guest compound between the β-chitin molecular chain sheets within the crystal. This intercalation compound cannot be produced merely by mixing the guest compound with the β-chitin. In order to interpose the guest compound between the lattice planes of the β-chitin molecular chain crystal, it is necessary to use one of the three methods described in the specification of the present application: (1) the immersing-in-melt method, (2) the immersing-in-solution method, or (3) the guest substitution method. In addition, the guest compound must meet the limitations recited in claim 1.

As shown by the X-ray diffraction date in Fig. 1 and Fig. 2, the spacing between the sheets of chitin molecular chains is increased as a result of the insertion of the guest molecules between the sheets. The claimed complex is useful as a drug delivery system in which the drug is the guest compound introduced into the β-chitin crystal lattice.



The intercalation compound recited in the claims is represented by the figure in the lower right of the above set of drawings, which shows the molecules of the guest compound inserted between the sheets of β-chitin.

Rejection under 35 USC §102

Claims 1-5 and 7 were rejected under 35 USC §102(b) as being anticipated by McCandliss et al. as evidenced by Falini et al. McCandliss et al. is cited for disclosing a naturally occurring chitin-protein complex which may be obtained from "invertebrate marine organisms having visible shells" (col. 5, lines 40-41). McCandliss et al. cites as examples of such organisms "crustaceans, mollusks, marine benthic organisms and krill fish." Since McCandliss et al. does not indicate which form of chitin is contained in these organisms, Falini et al. is relied upon as evidence that one of the categories mentioned in McCandliss et al., namely mollusks, contains β-chitin.

Since McCandliss et al. does not disclose an intercalation structure as recited in claim 1, Falini et al. is cited for disclosing at page 2, lines 8-13, that the β-chitin from mollusk shells is sandwiched between protein layers, and this arrangement is stated in the final Office Action to be an "inclusion complex." Applicants respectfully traverse this interpretation of the teachings of Falini et al. The specific passage from Falini et al. (beginning at page 2, left column, line 8) which was cited in the Office Action reads as follows:

> *"In the nacre mollusk shell, the mineral phase forms inside a preformed organic matrix. X-ray and transmission electron microscopy (TEM) studies of the matrix in the mineralized tissue showed that it is composed of thin layers of β-chitin sandwiched between two thicker layers of silklike proteins, onto which acidic macromolecules rich in aspartic acide are adsorbed.[11,12] The fiber axis of the chitin and the silk proteins are perpendicular to each other and aligned with the a and b axes of the mineral phase...."*

Applicants emphasize again that the above structure disclosed in Falini et al. for the nacre mollusk shell is not an intercalation compound. This is particularly evident in the description of the axis of the silklike protein fibers as being perpendicular to the axis of chitin layers. The structure disclosed in Falini et al. clearly does not meet the terms of Applicants' claims which recite that the guest compound is introduced between the sheets of chitin molecular chains. Falini et al. describes a structure on a macro scale compared to the structure recited in Applicants' claims which specify a structure at the level of the crystal lattice of pure β-chitin, the guest compound being introduced into the crystal lattice so as to force apart the sheets of chitin molecular chains.

In conventional complexes of β-chitin and a protein, the association between the β-chitin and the protein is not at the level of the crystal lattice of β-chitin, but is on a macro level, as illustrated by the figure on the lower left of the above set of drawings. The chitin-protein complex of McCandliss et al. is such a macro composite obtained by mild acid hydrolysis to demineralize naturally occurring chitin-containing biomass.

In summary, Applicants submit that neither McCandliss et al. nor Falini et al. discloses a manufactured β-chitin complex comprising an intercalation compound defined by the crystal

lattice recited in the claims. It is respectfully requested that the rejection of claims 1-7 over McCandliss et al. be reconsidered and withdrawn.

Rejection under 35 USC §103

Claims 1-7 were rejected under 35 USC §103 as being unpatentable over Drohan et al. in view of Kim et al. Drohan et al. is cited for disclosing a supplemented chitin hydrogel wherein the hydrogel serves as a carrier vehicle for delivery of growth factors or other agents to an internal or external wound. Acknowledging that Drohan et al. does not specifically disclose the chitin to be β-chitin, the Office Action cites Kim et al. for teaching that β-chitin is a good candidate material for uses in medical implant devices, wound dressings, drug delivery, etc. (page 2368, left column, lines 13-17.) The conclusion is set forth in the Office Action that it "would have been obvious to one of ordinary skill in the art ... to combine the invention of Drohan et al. with the teaching in Kim et al. of the specific β-chitin."

As previously stated, Applicants submit that even if one of ordinary skill in the art were to be motivated to combine the teachings of Drohan et al. with those of Kim et al. as suggested in the Office Action, the result would not be the manufactured β-chitin complex claimed herein. No combination of the teachings of these two references would lead to a complex having the modified β-chitin crystal lattice recited in the claims, in which a specifically defined guest compound has been introduced into the spaces between the stacks of sheets of chitin molecular chains which form the crystal lattice of β-chitin.

A reason given by Kim et al. for identifying β-chitin as a good candidate material for the uses mentioned in the Office Action is that "β-chitin showed much higher reactivity and availability as a starting material for facile chemical modifications" (Page 2368, left column, lines 12-15.) Kim et al. report that they had previously "prepared and characterized a semi-interpenetrating polymer network hydrogel membrane composed of β-chitin and poly(ethylene glycol) diacrylate macromer for possible application in biomedical areas. (Page 2368, left column, lines 17-21.) In other words, Kim et al. report having previously taken advantage of the reactivity of β-chitin to prepare this polymer network. The reactivity of β-chitin is referred to again at page 2370, paragraph bridging the left and right columns, in the context of the discussion of the hydrophilic nature of β-chitin being an advantage. Kim et al. report that clear

solutions of β-chitin in dimethylacetamide-LiCl and dichloroacetic acid-formic acid mixture have been obtained and used for the purpose of chemical modification under homogeneous reaction conditions.

In summary, Kim et al. considers β-chitin to be advantageous for these reasons:

- Water permeation into the crystalline region of β-chitin
- Hydrophilic nature of β-chitin facilitating solution in organic compounds;
- Chemical reactivity of β-chitin.

Kim et al. does not mention or even hint at the prospect of some compound other than water being "permeated" into the crystalline region of β-chitin. In other words, Kim et al. does not envision the introduction of a guest compound, as defined in the present claims, into the crystal lattice of β-chitin, as also recited in the claims. Therefore, even if one of ordinary skill in the art were to be led to combine the teachings of Kim et al. with those of Drohan et al., the result would not be the complex claimed by Applicants. In particular, neither reference teaches or suggests a method by which a complex as claimed by Applicants could be prepared. It is respectfully requested that the rejection of the claims over Drohan et al. in view of Kim et al. be reconsidered and withdrawn.

Applicants believe that the application is in condition for allowance. However, should the Examiner believe that there is any remaining issue and it may be resolved by telephone to place the application in condition for allowance, the Examiner is invited to contact Applicants' attorney at the telephone number listed below.

In the event this reply is not considered to be filed timely, Applicants hereby petition for an appropriate extension of the time period for filing the accompanying Request for Continued Examination and this reply. The fee for such petition for extension of time may be charged to Deposit Account No. 502081.

Respectfully submitted,

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